

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
2 August 2001 (02.08.2001)

PCT

(10) International Publication Number
WO 01/55346 A3

- (51) International Patent Classification⁷: **G01N 33/574**, C12N 5/00
- (21) International Application Number: **PCT/EP01/00717**
- (22) International Filing Date: 23 January 2001 (23.01.2001)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
100 02 803.9 24 January 2000 (24.01.2000) DE
- (71) Applicant (for all designated States except US): **DAKO A/S** [DK/DK]; Produktionsvej 42, DK-2600 Glostrup (DK).
- (72) Inventor; and
- (75) Inventor/Applicant (for US only): **GERDES, Johannes** [DE/DE]; Steinfeld 79, 23858 Feldhorst (DE).
- (74) Agents: **FÜCHSLE, Klaus et al.**; Hoffmann . Eitle. Arabellastrasse 4, 81925 München (DE).
- (81) Designated States (national): CA, JP, US.
- (84) Designated States (regional): European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR).
- Published:
— with international search report
- (88) Date of publication of the international search report:
14 February 2002
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



WO 01/55346 A3

(54) Title: **SYSTEM FOR THE INTERNAL QUALITATIVE AND QUANTITATIVE VALIDATION OF MARKER INDICES**

(57) Abstract: The present invention relates to the qualitative and quantitative validation of marker indices, especially for medical diagnosis and particularly for the determination of the growth fraction in a sample with antibodies against the Ki-67 protein. Diagnostic kit for the quantification of a cell fraction labeled by a marker for in vitro diagnosis, characterized in that a pseudo-tissue is used for the intra- and inter-assay standardization of the marker index.

INTERNATIONAL SEARCH REPORT

International Application No

/EP 01/00717

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/574 C12N5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 478 739 A (SLIVKA SANDRA R ET AL) 26 December 1995 (1995-12-26) column 5, line 40 -column 9, line 35; figures 7,8 column 14, line 14 - line 24 column 16, line 54 -column 17, line 51 column 21, line 31 - line 38 ---	1-8, 17-19,24
A	WO 98 08976 A (QUAY STEVEN C) 5 March 1998 (1998-03-05) page 19, line 30 -page 20, line 8 page 26, line 4 - line 20 page 29, line 1 - line 29 page 36, line 2 - line 14 --- -/--	9-16, 20-23

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

17 July 2001

Date of mailing of the international search report

24/07/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Schönwasser, D

INTERNATIONAL SEARCH REPORT

International Application No

/EP 01/00717

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>EP 0 695 760 A (HOFFMANN LA ROCHE) 7 February 1996 (1996-02-07) page 6, line 57 -page 7, line 6 page 7, line 21 - line 28 page 8, line 6 - line 8 -----</p>	<p>9-16, 20-23</p>

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-11,13-24 searched incompletely

Present claims 1-11 and 13-24 relate to an pseudo-tissues, diagnostic kits, analytical methods, detection systems and uses thereof which are characterized by an extremely large number of possible cell markers. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of these markers. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to Ki-67 markers as mentioned in claims 4 and 12 and e.g. on page 3, line 15 -page 4, line 35 of the application and in the examples.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

/EP 01/00717

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5478739	A	26-12-1995	NONE	
WO 9808976	A	05-03-1998	US 5798266 A	25-08-1998
			AU 4085097 A	19-03-1998
			EP 0932699 A	04-08-1999
			JP 2000514564 T	31-10-2000
EP 0695760	A	07-02-1996	WO 9604302 A	15-02-1996